17. (Amended) The composition of claim [1 or] 15 wherein the acetylated mono-glyceride is a fully acetylated mono-glyceride prepared from unsaturated mono-glyceride.

REMARKS

The Examiner has rejected Claims 1, 15 to 21 under 35 U.S.C. 103(a) as being unpatentable over Cavanak (US 5,639,724) in view of Woo (US 5,589,455).

Referring now to United States Patent No. 5,639,724 to Cavanak hereinafter referred to as Cavanak there is taught at column 19, line 6 onward that acetylated fatty acid mono- and di-glycerides such as commercially available under the trade name MYVACET, and in particular mono- and di-acetylated fatty acid monoglycerides, for example mono- and di-acetylated stearic acid monoglycerides such as MYVACET 9-40 and MYVACET 9-45 are of particular utility in that they are mixed glycerol fatty acid partial esters, for example products comprising fatty acid mono- and di-glycerides. There is no discussion within the Cavanak reference with regard to the advantages of acetylated monoglycerides perse not in combination with di-glycerides. This distinction is discussed at page 3 at the bottom thereof and Applicant's disclosure discussing the prior art mixing the various mono- and di-glycerides in relation to page 7 of Applicant's teaching setting out the advantage of acetylated monoglycerides over those in the prior art being low cost and that they are effective good solvents for cyclosporins reducing the amount of lipophilic solvent required and/or reducing the need for a hydrophilic co-solvent, but if required they are readily intradissolved with preferred hydrophilic co-solvents, and finally that they become readily dispersible into emulsions or microemulsions upon inclusion of suitable surfactant. Because of the aforesaid properties, the acceptable emulsion preconcentrates or micro-emulsion preconcentrates can be made using only cyclosporine acetylated monoglycerides and a surfactant. This limitation is set out in amended Claim 1 as set out below.

"A pharmaceutical composition comprising an emulsion preconcentrate including a cyclosporin dissolved in a solvent system comprising substantially fully acetylated monoglycerides having a minimum acetylation of 96%, a hydrophilic organic solvent and at least two surfactants."

Clearly, there is no teaching within Cavanak to provide such an emulsion preconcentrate. There is no motivation within Cavanak to provide a emulsion preconcentrate and further a limitation of the emulsion of the preconcentrate would include fully acetylated mono-glycerides and not combinations of mono- and di-glycerides as per the teachings of Cavanak. There is no teaching in Cavanak and for that matter neither in Woo which is to be discussed hereinafter, related to the advantages set out above taken from Applicant's disclosure, the use of fully acetylated mono-glycerides. Cavanak teaches various permutations and combinations which respectively do not focus in on an Applicant's invention. Further, in fact if one were to focus Cavanak by referring to the claims, clearly the invention is specified as including a mixture of mono-glycerides and di-glycerides and tri-glycerides. Cavanak therefore is silent on Applicant's invention as set out in the amended claim above.

Further, referring to United States Patent No. 5,589,455 hereinafter referred to as Woo there is taught a micro-emulsion concentrate containing cyclosporine as the active with no discussion whatsoever of utilizing acetylated monoglycerides as liquifilic solvent for cyclosporine. The Woo reference teaches in fact, micro-emulsion concentrate containing cyclosporine in combination with a carrier consisting of a dimethylisosorbide as a co-surfactant refined fish oil as an oil component and a surfactant which is suitable for formulation into soft capsules for oral administration. Refined fish oil is defined as being ideally fit for absorption, cyclosporin since it contains a highly saturated fatty acid, such as EPA and DHA. This is not part of Applicant's teachings and in fact, Applicant is using unsaturated acetylated mono-glycerides which point specifically in the opposite direction. Woo also teaches mixtures of various fatty acids and primary alcohols, for example, medium chain fatty acid tri-glyceride and fatty acid mono-glyceride as the oral component. Further, there is no discussion of the advantages of utilizing within the

micro-emulsion, the small droplets and just how small those droplets might be considered to be in order to get improved transmittance as a measurement for clarity, with higher transmittance indicating smaller droplet size and finer emulsion or micro-emulsion as identified on page 12 of Applicant's disclosure which result in an improvement of the uptake of cyclosporin into the system as a result. This issue is simply not addressed within Woo as set out in Applicant's Claim 15.

> "A pharmaceutical composition comprising a micro emulsion preconcentrate having a droplet size of substantially less than 2000 A, including a cyclosporin dissolved in an acetylated mono-glyceride lipophilic solvent, and a surfactant."

Although Woo may identify the use of a micro-emulsion concentrate there is no discussion of the size of the droplets in spite of the fact that one alternative it is stated that the oils might be used in single form, that is to say, fatty acid mono-glyceride. Clearly, though there is no discussion of an acetylated mono-glycerides in combination with at least two surfactants as in Applicant's Claim 1 set out above.

At page 9 of Applicant's disclosure, particularly Applicant has found surprisingly that the preferred surfactants have a synergistic action with other surfactants so that inclusion of a second surfactant as a co-surfactant can reduce the total amount of surfactant need without loss of effectiveness in enabling dispersion to an emulsion or a micro-emulsion. Therefore, in Claim 1 Applicant has included a limitation of at least two surfactants as supported in Applicant's disclosure which clearly identifies over either Woo or Cavanak again set out below.

> *1. A pharmaceutical composition comprising an emulsion preconcentrate including a cyclosporin dissolved in a solvent system comprising substantially fully acetylated monoglycerides having a minimum acetylation of 96%, a hydrophilic organic solvent and at least two surfactants.*
>
> *15. A pharmaceutical composition comprising a micro emulsion preconcentrate having a droplet size of substantially less than 2000 A, including a cyclosporin dissolved in an acetylated mono-glyceride lipophilic solvent, and a surfactant.*

Therefore, there is nothing within the teachings of either Cavanak or Woo alone or in combination which would result in Applicant's claims, and according to accepted Juris prudence provided with Applicant's preliminary amendment to which the Examiner is referred to and which is incorporated by reference in it's entirety, it is clear that using Applicant's disclosure as a blueprint it is entirely unacceptable in relying on a 20/20 hindsight reconstruction as set out in Hodosh and Brock Drug Company, and other examples such as in re Roffet to which the Examiner is referred to for further evaluation. There is nothing within the teachings of Cavanak nor Woo, nor a combination of Cavanak and Woo that would motivate one of ordinary skill in the art to arrive at Applicant's independent claims 1 and 15 as set out above. There is no motivation in either reference to do so, and although these references may broadly be within the same discipline as stated by the Examiner, the alleged obviousness of the combination is now mute in view of Applicant's amendments, and full reconsideration is requested.

The Examiner has rejected Claims 1 and 15-21 under 35 U.S.C. 101 as allegedly claiming the same invention as that of Claims 1-9 of prior U.S. Patent No. 6,159,933. The Examiner has requested the filing of a Terminal Disclaimer. Applicant believes that a Terminal Disclaimer is not appropriate, since the rejection under 35 U.S.C. 101 would not be overcome by filing same.

A. Statutory Double Patenting - 35 U.S.C. 101

In determining whether a statutory basis for a double patenting rejection exists, the question to be asked is: Is the same invention being claimed twice? 35 U.S.C. 101 prevents two patents from issuing on the same invention. "Same invention" means identical subject matter. Miller v. Eagle Mfg. Co., 151 U.S. 186 (1984); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957).

A reliable test for double patenting under 35 U.S.C. 101 is whether a claim in the application could be literally infringed without literally infringing a corresponding claim in the patent. In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970). Is there an embodiment of the invention that falls within the scope of one claim, but not the other? If there is such an embodiment, then identical subject matter is not defined by both claims and statutory double

patenting would not exist. For example, the invention defined by a claim reciting a compound having a "halogen" substituent is not identical to or substantively the same as a claim reciting the same compound except having a "chlorine" substituent in place of the halogen because "halogen" is broader than "chlorine". On the other hand, claims may be differently worded and still define the same invention. Thus, a claim reciting a widget having a length of "36 inches" defines the same invention as a claim reciting the same widget having a length of "3 feet".

35 U.S.C. 101, Statutory Basis for Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefore ..." (Emphasis added). Thus, the term "same invention", in this context, means an invention drawn to identical subject matter. See Miller v. Eagle Mfg. Co., 151 U.S. 186 (1894); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957).

A. Same-Invention Double Patenting

Under 35 U.S.C. Section 101, a person is entitled to a patent. Thus, the first question to be asked by the Examiner in establishing a prima facie case of double patenting is whether the same invention is being claimed twice.

In re Vogel is an exemplary case of distinguishing same-invention (statutory) double patenting from obviousness-type (nonstatutory) double patenting. Vogel had patented a method of preparing pork products and then filed another application with claims directed to a process of packaging meat. The claims in this second application were based on Vogel's discovery that spoilage and discoloration of meat were markedly accelerated if the meat was allowed to reach ambient temperature before packaging. A dependent claim was directed to a similar process specifically limited to beef.

During the appeal before the Board, the Examiner's answer asserted that the claimed process steps were essentially the same as in the patented process claims, and that the choice of beef rather than pork "is of no patentable significance since this would appear to be a judicious choice of available meat products, well within the ordinary skill of the art, and particularly so, in the absence of any unusual or unobvious result." The Board held that the appealed claims merely extended the pork process to beef, and that this was not a patentable advance.

On appeal, the CCPA reversed. In the opinion, the CCPA suggested a restatement of the law was necessary:

> The first question in the analysis is: Is the same invention being claimed twice? 35 U.S.C. 101 prevents two patents from issuing on the same invention .... By "same invention" we mean identical subject matter. Thus the invention defined by a claim reciting "halogen" is not the *same* as that defined by a claim reciting "chlorine", because the former is broader than the latter. On the other hand, claims may be differently worded and still define the same invention. Thus a claim reciting a length of "thirty-six inches" defines the same invention as a claim reciting a length of "three feet", if all other limitations are identical ... A good test, and probably the only objective test, for "same invention", is whether one of the claims could be literally infringed without literally infringing the other. If it could be, the claims do not define identically the same invention.

Thus, *Vogel* teaches that the test for same-invention double patenting is whether one of the claims in the first patent could be literally infringed without literally infringing one of the claims in the other patent. In establishing the literal infringement test, the CCPA has rejected the idea that a standard such as colorable variation be used to distinguish between inventions. Rather, the CCPA has concluded that for double patenting, inventions are either the same, obvious variations, or nonobvious variations. Hence, any reference to differences between inventions other than "obvious" or nonobvious" differences are inappropriate with respect to a same-invention double patenting rejection.

Thus, an Examiner asserting a same-invention double patenting rejection must show that the same invention is being claimed twice. To establish this type of double patenting, the Examiner must show that the claims in the issued patent and the pending application cannot be literally infringed without literally infringing one another.

Since the rejection lacks the necessary literal infringement analysis, Applicant requests that the rejection be withdrawn because the Examiner has failed to make a prima facie case of same-invention double patenting under *Vogel* especially in view of the amendments above.

Further to the teachings of Sherman, United States Patent No. 6,159,933 hereinafter referred to as Sherman, there is claimed in Claim 1 as allowed,

> *"A pharmaceutical composition, wherein said composition is an emulsion preconcentrate, comprising a cyclosporine dissolved in a solvent system comprising propylene carbonate, a lipophilic solvent selected from glycerides, and at least one surfactant."*

All of the other claims are dependent claims which depend on Claim 1.

Applicant has claimed in amended Claim 1 and 15 as follows,

> *1. A pharmaceutical composition comprising an emulsion preconcentrate including a cyclosporin dissolved in a solvent system comprising substantially fully acetylated monoglycerides having a minimum acetylation of 96%, a hydrophilic organic solvent and at least two surfactants.*
>
> *15. A pharmaceutical composition comprising a micro emulsion preconcentrate having a droplet size of substantially less than 2000 A, including a cyclosporin dissolved in an acetylated mono-glyceride lipophilic solvent, and a surfactant.*

Clearly, therefore Applicant in reviewing the test in re: Vogel reversed in the CCPA sets out above the inventions claimed by Sherman and claimed by Applicant. Under 35 U.S.C. 101, "same invention" means identical subject matter. The same invention must be claimed twice. The term "same invention" means an invention drawn to identical subject matter. The test therefore is clear and that is, can claim 1 set out above from Sherman said to literally infringe claim 1 or 15 of Applicant set out above. The converse therefore would also have to be true and that is would claim 1 and 15 of the present application infringe Sherman. The claims therefore as amended do not satisfy this literal infringement analysis and Applicant therefore has shown that with his amendments of this response the Examiner's statutory double patenting rejection is therefore mute in view of the amendments made, and full reconsideration and withdrawal thereof is requested. Since such a rejection cannot be satisfied with a Terminal Disclaimer none is being filed in spite of the Examiner's statement in paragraph 5 of her report on page 4 dated August 2, 2001, since there is no rejection based on a non-statutory double patenting basis.

In summary therefore, Applicant has addressed each and every issue identified by the Examiner by providing argument and amendments. With reference to the traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, for Section 103 the scope and content of Cavanak and Woo have been determined, the differences between those references and claims 1 and 15 as amended have been. The patentability of the claims at hand stems from the fact that the specific combination as setout above in amended claims 1 and 15 was not disclosed in relation to fully acetylated monoglycerides and the advantages thereof set out in applicant's disclosure as abovementioned, used in cooperation with at least

two surfactants. Further there is no teaching in the prior art related to the use of microemulsion preconcentrates having a droplet size of less than 2000 Angstroms.

See Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n5, 229 U.S.P.Q. 182, 187 n5 (Fed. Cir. 1986) (listing the "following tenets of patent law that must be adhered to when applying § 103: (1) the claimed invention must be considered as a whole . . . (2) the references must be considered as a whole and suggest the desirability and thus the obviousness of making the combination . . . (3) the references must be viewed without the benefit of hindsight vision afforded by the claimed invention . . . (4) 'ought to be tried' is not the standard with which obviousness is determined . . . and (5) the presumption of validity remains constant and intact throughout litigation"). For a topical outline and case tables covering the decisions of the Federal Circuit, see the separate *Guide to the Patent-Related Decisions of the Court of Appeals for the Federal Circuit* in Volume 6 of this treatise. See also Dunner, ed., "The United States Court of Appeals for the Federal Circuit - Its First Three Years," 13 AIPLA Q.J. 185 (1985); Mintz & Racine, "Anticipation and Obviousness in the Federal Circuit," 13 AIPLA Q.J. 195 (1985).

In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

> *"Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious. The court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."*

Further in re Vaeck , 947 F.2d 488,20 USPQ2d 1438 (Fed. Cir. 1991):

> "Rejection of claimed subject matter as obvious under 35 USC 103 in view of combination of prior art references requires consideration of whether prior art would have suggested to those of ordinary skill in art that they should make claimed composition or device, or carry out claimed process, and whether prior art would also have revealed that such person would have reasonable expectation of success; both suggestion and reasonable expectation of success must be founded in prior art, not in applicant's disclosure."

Further the Examiner is referred to the following excerpted case law recently reviewed.

In Re: Rouffet, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998)

> *"As this court has stated, "virtually all [inventions] are combinations of old elements." Environmental Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); see also Richdel, Inc. v. Sunspool Corp., 714 F.2d 1573, 1579-80, 219 USPQ 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old elements."). Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be "an illogical and inappropriate process by which to determine patentability." Sensonics, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ 2d 1551, 1554 (Fed. Cir. 1996).*
>
> *To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.*

Full reconsideration and withdrawal of the rejections is requested.

Attached hereto as **Exhibit A** is a marked-up version of the changes made to the claims by the present amendment. Exhibit A is entitled "EXHIBIT A - CLAIMS WITH MARKINGS TO SHOW CHANGES".

Attached hereto as **Exhibit B** is a clean set of all pending claims following entry of this amendment. Exhibit B is entitled: "EXHIBIT B - CLEAN SET OF ALL PENDING CLAIMS FOLLOWING ENTRY OF THE PRESENT AMENDMENT". All

of the currently pending claims are consolidated in this list for the convenience of the Examiner.

If there are any fees required with respect to the above-identified matters, Applicant authorizes the Commissioner to access Applicant Agent's Deposit Account No. 08-3255 and advise Applicant's Agent.

If the Examiner has any questions, she is respectfully requested to contact Applicants' Agent, Neil H. Hughes at (905) 771-6414 at her convenience.

Respectfully submitted,

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NHH:mse
Enclosures

Amendment A
U.S. Application Serial No. 09/783,969
Group Art Unit 1614

EXHIBIT A

CLAIMS WITH MARKINGS TO SHOW CHANGES

Please amend the claims as follows.

1. (Amended) A pharmaceutical composition [in the form of an emulsion preconcentrate] comprising an emulsion preconcentrate including a cyclosporin dissolved in a solvent system comprising substantially fully acetylated monoglycerides having a minimum acetylation of 96%, a hydrophilic organic solvent and [a] at least two surfactants.

15. (Amended) A pharmaceutical composition [in the form of an emulsion preconcentrate] comprising a micro emulsion preconcentrate having a droplet size of substantially less than 2000 Å, including a cyclosporin dissolved in an acetylated monoglyceride lipophilic solvent, and a surfactant.

16. (Amended) The composition of claim 1 [or 15] in the form of a microemulsion preconcentrate.

17. (Amended) The composition of claim [1 or] 15 wherein the acetylated monoglyceride is a fully acetylated monoglyceride prepared from unsaturated monoglyceride.